Remarks

This is in response to the Office Action dated January 11, 2010 in the above-identified patent application.

I. Status of the Claims.

Claims 53-71 and 76-79 were pending for purposes of the instant Office Action. Claims 72-75 were previously canceled, being drawn to non-elected methods of groups II and III, pursuant to the earlier restriction requirement. Applicants appreciate the Examiner's recognition of the inadvertent omission of claim 74 from the restriction requirement and the continued consideration of claim 55, as intended.

Claims 53-65, 67-71 and 76-80, as amended, are provided in the Listing of Claims, above. Claim 66 has been canceled and certain new amendments have been made to the pending claims. In addition, subject matter objected to in claim 56 has been removed from that claim and is now presented in new claim 80. Accordingly, claims 53-65, 67-71 and 76-80 are now pending. It is respectfully submitted that no new matter is presented by the above amendments. Reconsideration of the pending claims is respectfully requested.

II. *Withdrawn Rejections*

Applicants acknowledge the withdrawal of the rejections of claims 11 and 12 (under 35 USC §112), the rejection of claims 1, 3-4, 6-10, 13-34, 39-47, and 49-50 (under 35 USC §103(a) over Lieberman in view of Geller) and the rejection of claims 35-38 and 51-52 (under 35 USC §103(a) over Lieberman in view of Lofroth) pursuant to applicants' cancellation of those claims.

III. *New Grounds of Objection/Rejection*

The Office Action notes that the subject application is a US national-stage filing under 35 USC 371 containing subject matter disclosed in International Application PCT/US05/42120. As shown in the Amendment to the Specification, above, applicants have inserted into the specification the claim to priority of the International Application, as required. Because the priority claim was submitted in the oath or declaration in the subject application, and was

recognized in the Filing Receipt dated June 17, 2008, applicants believe a petition and fee to amend the specification are not required.

Claim Objections

Claims 54-56 are objected to because of the informality of a missing quotation mark before the word "below." The missing quotation mark is now provided by the amendments shown in the above Listing of Claims. Applicants respectfully request withdrawal of this objection.

IV. Claim Rejections under 35 USC §112.

Claims 56-66, 69-71, and 78-79 are rejected under 35 USC §112, second paragraph, as being indefinite. The Examiner correctly notes that claims 56-60, 62-66, 69-71, and 78-79 are directed to a composition that contains an effective amount of a drug or drugs (B) or (C). However, the previously presented Markush group recited compositions having a tablet structure of A-I-A and A-I-A-I, i.e., tablet structures that did not include a drug or drugs (B) or (C). To address this indefiniteness issue, applicants have amended independent claim 56 to remove the recitation of tablet structures A-I-A and A-I-A-I from that claim. Accordingly, applicants believe that claims 56-66, 69-71, and 78-79 are now definite and meet all requirements of 35 USC §112. The Examiner's helpful comments are greatly appreciated. Reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph, is respectfully requested.

Notably, applicants have added new claim 80, which includes tablet structures A-I-A and A-I-A-I. Support for these claims was provided in the original claims, as filed, and in the drawings as originally submitted.

Claims 61 and 62 were considered indefinite due to the recitation of the term "solubility modifiers." This term has been deleted from claims 61 and 62. Reconsideration and withdrawal of this rejection is also respectfully requested in view of the amendment to these claims.

Claim 66 was rejected as being unclear for its recitation of "a score having a depth of at least 70% of the horizontal dimension or width of the segment." In view of the cancellation of claim 66, applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections – 35 USC §103

Claims 53-71 and 76-79 stand rejected under 35 USC §103(a) as being unpatentable over Lieberman (Pharmaceutical Dosage Forms – tablets, 1990) in view of Ullman (US Pat. No. 4,215,104). This rejection is respectfully traversed.

Applicants respectfully submit that the cited references of Lieberman and Ullman describe tablets that are completely different than the tablets claimed in the subject invention. First, the Office Action admits that "Lieberman acknowledges that traditional scores result in significant variation in drug dose." This statement unequivocally corroborates applicants' position because, even with traditional scores, the tablets of the subject invention overcome the well-known and well-recognized problem of significant variation in drug dose following tablet splitting.

The relative breaking accuracy of certain embodiments of tablets according to the present invention was compared to the breaking accuracy of prior art scored tablets. The tests showed that the tablets of the present invention had a maximum deviation, between tablet halves, below 3.5%. In the case of prior art scored tablets, the deviation was observed to be as high as 20% for certain tablets. In addition, 55 of the 90 prior art test tablets could not be split by the volunteers, while all of the tablets of the invention could be split by the volunteers. Attached to this Amendment is the Declaration of Elliot Hahn, filed under the provisions of 37 CFR§1.132, stating the results of actual tests, described above, that were conducted to test the relative breaking accuracy.

The tests were evaluated by weighing the tablets after they were broken by hand. These results, which could not be predicted from any disclosure in Lieberman or Ullman, validate the concept of the invention.

Moreover, in certain other embodiments of tablets of the subject invention, the fact that breaking of those tablets does not result in significant variation in the drug dose is due solely

to the unique configuration of those tablets rather than any modified or non-traditional score placed in those tablets. Certain embodiments of applicants' tablets *do have* traditional scores, and those traditionally scored tablets produce the same unique advantage – no significant variation in drug dose after tablet splitting. This advantage results from the novel and unobvious tablet configuration as expressly recited in the claims.

Even if the deep score of the tablet of claim 53 (a score greater than 50% of the thickness of the active layer) is considered to be a "non-traditional" score, the unexpected advantage exhibited by the tablet of claim 53 depends on its unique, layered configuration comprising (a) an active segment and (b) an inactive outer segment. Thus, the presence of the inactive outer segment (which allows the tablet to contain the deep score without affecting the integrity of the tablet during manufacture, shipping or storage) is a claimed aspect of the tablet configuration that cannot be minimized or overlooked when reviewing the claim against the prior art. This unique inactive outer segment configuration, in combination with the deep score, facilitates breaking of the tablet and splitting of the dose *without significant variation in the dose*. In fact, a unique advantage of certain embodiments of a tablet within the scope of claim 53 allows splitting of the dose without *any* variation in the doses contained in each tablet half ("tablette").

Moreover, a tablet of claims 54-56, having a height greater than its width (i.e., a taller-than-wide tablet), also provides its advantage of accurate dose splitting due to the unique tablet configuration – not due to any modification to the score. The claimed taller-than-wide tablet contains an inactive segment between two active segments wherein the inactive segment advantageously serves as a breaking segment. Breaking through that inactive middle segment – and allowing the tablet to break through that inactive segment only (not through any active segment), the dose can be divided without significant variation in the resultant partial doses because there is no breakage or other detrimental effect occurring to the active segments containing the partial doses.

Therefore, Lieberman does not simply fail "to teach how deep of a score a tablet should have," as asserted in the Office Action; rather, Lieberman fails to describe a tablet having an inactive outer segment as expressly recited in claim 53, *and* Lieberman further fails to

describe a taller-than-wide tablet of claims 54-56. Lieberman is limited in its teaching to a conventional (wider-than-tall), three-layered tablet having a thin, inactive separating layer disposed between two incompatible active layers. The inactive layer of Lieberman cannot serve as a breaking segment that provides accurate and precise dose splitting. Lieberman never hints of providing an advantage of tablet splitting without variation in dosage. Therefore, Lieberman fails to teach or suggest anything close to the claimed tablets.

In addition, there is no teaching or suggestion in Lieberman to modify the three-layer tablet of Lieberman to provide a tablet of claim 53, having an active layer and an inactive outer layer serving as a breaking segment. Nor is there any teaching or suggestion in Lieberman to modify the conventional wider-than-tall tablet to provide a taller-than-wide tablet having an inactive middle segment that serves as a breaking segment. Both of these structural aspects of the subject invention are unique to the claimed invention and are unobvious in view of the prior art.

The Office Action then brings in the Ullman reference as teaching a multi-fractionable unitary tablet structure. However, Ullman does not disclose a tablet having more than one layer – only a single-layer tablet, compressed from a single homogeneous composition. Applicants respectfully traverse the applicability of the single-layer tablet of Ullman to the multi-layered tablet of Lieberman, or the claimed invention. The scoring aspect of the tablets described in Ullman, cannot cure the defects of Lieberman because Lieberman is defective in its teaching vis-a-vis the subject invention in ways that are not related to scoring of the tablets, as explained above.

In referring to Ullman, the Office Action erroneously states that "[a]s can be seen in figure 3, the tablet can have a height which is greater that the width of the tablet, and the center section is thicker that the thickness of both the top and bottom sections together." This characterization of the height and width dimensions of the Ullman tablet is not accurate. The dimensions of the Ullman tablet, as referred to by the Examiner, do not comport with the carefully defined height and width dimensions for the tablets of the subject application.

In drafting the subject application, applicants took great care to define precisely, and without confusion, the meaning of "height" and "width" dimensions as they apply to the claimed tablets. Specifically, the subject application, at page 10, lines 1-15 provides:

> said [tablet] height being measured vertically from the top to the bottom of said tablet while it is in the tablet die in which it is fully compressed, after said compression has been completed; and said width being measured as the greatest horizontal dimension of the tablet at a location halfway between said top and said bottom of said tablet, except that when the horizontal cross-section of said tablet is substantially rectangular, the width is defined by locating the two shorter sides of the perimeter of said horizontal cross-section, and measuring the length of a line that is at right angle to said shorter sides. The terms "vertical" and "horizontal" ("horizontal" is also referred to as "transverse") axis of the tablets of the invention are determined by and have the same orientation as that of the tablet die in which the tablet is compressed in a tablet press or other tabletting machine ("tablet press" herein), and the order of entry of granulations into the die.

Those definitions are also expressly referenced in the clams, themselves, to further reduce any confusion regarding the dimensions of the claimed tablets. Moreover, in providing the definitions, applicants even go so far as to contemplate a substantially rectangular tablet as shown in Ullman, and further define the width by indicating that the two shorter sides are first located, and the length of the line perpendicular to those shorter sides is measured as the width.

To summarize, the dimensions of the claimed tablets are measured while the tablet is in the die, and are not dependent on the orientation of the tablet when removed from the die. Notably, the height is the vertical dimension from top to bottom, and the width is measured as the greatest horizontal dimension, as the tablet is oriented in the die. Thus, applying the definitions provided in the subject application to a tablet of Ullman, the greatest horizontal dimension (width) is clearly much greater than the height of the tablet. The height of the Ullman tablet, measured from top 40 to bottom 56 in Figure 3, in all cases, is less than the "greatest horizontal dimension," or "width," measured from one end to the other end, e.g., end face 46 to end face 44 as shown in Figures 1 and 2 of Ullman. It is further noted that the reference numbers of Figure 3 must be read in light of Figure 2, which shows a "top" view, which indicates the top and bottom of the tablet as it is compressed in the tablet die.

Therefore, in contradistinction to the assertion made in the instant Office Action, Ullman does not show, or otherwise teach or suggest, a taller-than-wide tablet.

The Office Action asserts that, a person of ordinary skill would be motivated to utilize the superior score of Ullman with the layered tablet of Lieberman, and that there "would have been a reasonable expectation of success since both Lieberman and Ullman are teaching scored tablets." However, in view of the limitations of both of the cited references, there would have been no success at arriving at the claimed invention. Providing a score of Ullman in a layered tablet of Lieberman would result in a scored, conventional (wider-than-tall), three-layered tablet. This combined Lieberman/Ullman tablet could never be broken without affecting the partial doses in the divided tablet portions because the conventional wider-than-tall tablet breaks through all layers simultaneously, and cannot be readily split through an inactive layer only, as is achieved by the claimed tablets.

The distinction between breaking a taller-than-wide layered tablet of the subject invention and breaking a conventional wider-than-tall layered tablet (e.g., as described in Lieberman), is illustrated below:

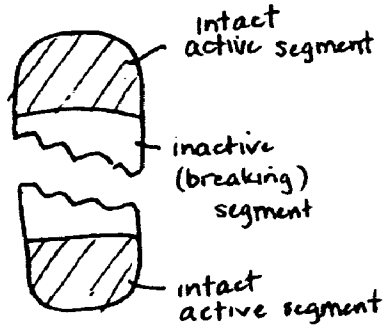

FIG. A. Breaking of a taller-than-wide layered tablet configuration

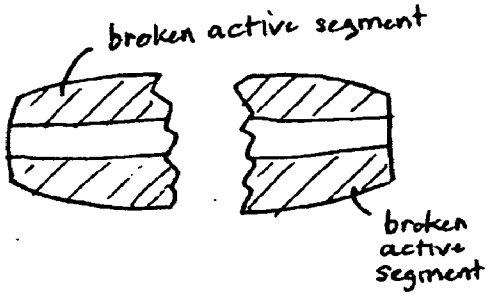

FIG.B. Breaking of a wider-than-tall layered tablet configuration

FIG. A illustrates the advantageous "breaking layer" formed by a middle inactive segment in a taller-than-wide tablet, providing breakage through the inactive layer and resulting in the active segments remaining intact – even if the break is not exactly through the midline. By contrast, a wider-than-tall layered tablet cannot provide the same advantageous break.

As shown in FIG. B, above, breaking a wider-than-tall tablet across its short axis results in breaking through all layers of the tablet. It is well known that the broken faces or edges of a tablet may chip or crumble, thus inevitably resulting in loss of mass, and therefore loss of some of the active ingredient, from a tablet layered in this configuration. This can be especially disadvantageous in highly potent drugs where such loss on breaking can be significant with regard to the dose actually administered.

The Office Action further asserts that it would have been obvious to utilize the top and bottom portion of Ullman tablet design for the incompatible ingredients of Lieberman. However, applicants fail to recognize any "top" or "bottom" *portion* of the Ullman single-layer tablet, especially a "top" or "bottom" portion as expressly defined for the subject tablet configurations. A fair reading of Ullman reveals that the described tablets do not have a "top" portion or "bottom" portion, but are homogeneous, single layer tablets compressed in a conventional wider-than-tall configuration. There is absolutely no teaching or suggestion in Ullman to provide multi-layered tablets, and any asserted motivation to combine Ullman with Lieberman is without support.

It is a fundamental concept in patent law that isolated teachings may not be extracted from a reference and used for unsupported contentions as to what a person of ordinary skill in the art would be motivated to do. Accordingly, one of ordinary skill in the art would not be able to use a "top" and "bottom" portion of the Ullman tablet that would allow breakage to occur in the inert barrier layer of Lieberman. Thus, any reasonable expectation of success is also absent from the combination of the references in this hypothetical.

Although the Office Action continues, and states that it would have been obvious to replace the incompatible drugs with compatible drugs in a three-layered tablet of Lieberman, such assertion fails because there is no motivation to include an inert barrier layer between two compatible drugs. An inert barrier layer between two compatible drugs in a conventional tablet is superfluous, and persons of ordinary skill in the tablet manufacturing arts would not be motivated to include an inert layer where it was not absolutely necessary because minimizing time, costs, and tablet size are factors that would motivate a person to <u>not</u> include the inert layer between compatible drug layers. Accordingly, applicants believe the

prior art teaches away from a tablet having an inert barrier layer between two compatible drug layers.

The only reasonable rationale for providing an inert barrier layer between two compatible drugs is to provide the advantageous breaking region, as disclosed in the subject application. No rationale for such configuration is provided in the prior art, including Lieberman and Ullman. Thus, the only conclusion that can be drawn from this assertion of obviousness is that it was arrived at based on the applicants' disclosure. However, hindsight reconstruction of the invention, using the disclosure of the subject application, is impermissible and cannot be used to support an obviousness rejection.

Additionally, the Office Action submits that the effective height of the inner segment is simply a result of size optimization. However, optimizing the size of the tablet is different than optimizing the size of the inner segment. There is nothing in the prior art that teaches or suggests modification of one segment and not the other two segments in a three-segment tablet. Applicants respectfully submit that it would be well recognized in the art that increasing the size of a whole tablet described in the prior art to provide an effective height for the inner segment consistent with the claimed invention would result in a tablet too large to swallow and, therefore, inoperable. Because the prior art does not teach or suggest size modification of only a single segment, there is no basis to make such assertion against the claimed invention.

In view of the above, reconsideration and withdrawal of the rejection under 35 USC §103(a) is respectfully urged.

V. Obviousness-type Double Patenting Rejection

Claims 53-71 and 76-79 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-9 of co-pending application Serial No. 10/598,344 in view of Lieberman and Ullman. Because the instant claims have been amended, and the claims of either the instant application or the cited '344 application have not yet been allowed, applicants respectfully submit that the issue of obviousness-type double patenting, and the submission of a terminal disclaimer to overcome

the obviousness-type double patenting rejection, will be considered upon indication of allowability for the claims.

In view of the above amendments to the claims and the accompanying Remarks, applicants believe that the pending claims, as amended, are in condition for allowance and respectfully request issuance of the Notice of Allowance.

Applicants invite the Examiner to contact the undersigned at the address and/or phone number provided below if clarification or additional information is needed on any of these matters.

Respectfully submitted,

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/Ted W. Whitlock/

Ted Whitlock
Registered Patent Attorney, PA
Registration No. 36,965

5323 SW 38th Avenue
Ft. Lauderdale, Florida 33312
Tel. 954-986-2119
Fax: 954-986-2120
Email: twpatent@msn.com